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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1632	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,150	CHIAUR ET AL.	
	Examiner	Art Unit	
	Wu-Cheng Winston Shen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-74* is/are pending in the application.

4a) Of the above claim(s) *56-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response received on 06/01/2007 has been entered. Claims 1-49 were cancelled. Claims 50-74 are pending. Claims 52 and 53 were amended.

Claims 56-74 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 50-55 are currently under examination.

This application 10/632,150 filed on July 30, 2003 is a DIV of 09/385,219 filed on 08/27/1999 patent No. 6720,181, which claims benefit of provisional applications 60/098,355 filed on 08/28/1998 and claims the benefits of 60/118,568 filed on 02/03/1999 and 60/124,449 filed on 03/15/1999.

Priority date

The subject matter of claims 50-55 of instant application requires nucleotide sequence of SEQ ID No: 9 (2076 nucleotides) that encodes the amino acid sequences of SEQ ID No: 10 (447 amino acid residues), asserted to be FBP5. The SEQ ID No: 9 and SEQ ID No: 10 of instant application are identical to the SEQ ID No: 9 and SEQ ID No: 10 disclosed in the parent application 09/385,219, filed on 08/27/1999, now US patent 6,720,181.

It is noted that the provisional application 60/098,355 filed on 08/28/1998 disclosed SEQ ID No: 10 (447 amino acid residues, see Fig, 7B, page 155 of 60/098,355) that is identical to SEQ ID No: 10 of instant application. However, SEQ ID No: 9, a cDNA encodes FBP5, disclosed in the provisional application 60/098,355 is 1409 nucleotide-long ending with TGA (See Fig, 7A, page 154 of 60/098,355), which is much shorter than SEQ ID No: 9 (2076

nucleotides) disclosed in instant application. Additional provisional application 60/118,568 filed on 02/03/1999 and 60/124,449 filed on 03/13/1999 disclosed the same SEQ ID No: 9, a cDNA encodes FBP5, as that disclosed in the provisional application 60/098,355.

Therefore, the priority date of claim 50 of instant application benefits from the priority dated back to the filing date of provisional application 60/098,355, 08/28/1998 because claim 50 only requires disclosure of SEQ ID No: 10 (447 amino acid residues).

The priority date of claims 51-55 is determined to be 08/27/1999, the filing date of parent application 09/385,219, now patent 6,720,181 as support for SEQ ID NO: 9 of the instant application is not found in either US Provisional Application 60/098,355 (filed on 08/28/1998), 60/118,568 (filed on 02/03/1999), or 60/124,449 (filed on 03/15/1999).

Claim Rejection - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

1. Claims 50-55 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Applicant's arguments filed 06/01/2007 have been fully considered and they are not persuasive. Previous rejection is ***maintained*** for the reasons of record advanced on pages 3-7 of the office action mailed on 12/01/2006.

Applicant's arguments

With regard to whether nucleotide sequence SEQ ID No: 9 (which is asserted to encode amino acid SEQ ID No: 10) has credible, specific, and substantial utility, Applicant argues the following: **(i)** The Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." Brooktree Corp. v. Advanced Micro Devices, Inc., 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401 (Fed. Cir. 1992), emphasis added. See also Cross" v. Iizuka (753 F.2d 1040, 224 U.S.P.Q. 739, 748 (Fed. Cir. 1985) (stating that "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101") (emphasis added); **(ii)** The specification has asserted that the nucleotide sequence set forth in SEQ ID NO: 9 encodes a novel ubiquitin ligase comprising an F-box motif, **(iii)** The specification provides numerous specific, substantial, and credible utilities for the claimed nucleic acid molecules comprising nucleic acid sequence of *SEQ ID NO: 9 which is the cDNA sequence of FBP5, a novel ubiquitin ligase F-Box protein.* Deregulation of FBPs is implicated in cancer development (specification at pages 3, line 3 to page 4, line 7). The claimed inventions indeed have specific utilities which are in contrast with a general utility that would be applicable to any nucleic acid molecules, such as expressed sequence tags (ESTs), which have no specific DNA target. In re Fisher, 421 F.3d 1365, 1371, 76 U.S.P.Q.2d 1225, 1230 (Fed. Cir. 2005). For instance, the specification at page 56, line 35 to page 57, line 7 teaches that the nucleic acid molecules of the present invention can be used as *hybridization probes* for detecting FBP5; **(iv)** Applicants argue that an invention has substantial utility even though further research needs to be performed. For example, an assay that measures the presence of a material, which has a stated correlation to a predisposition to the onset of a particular disease condition, would also define a "real world" context of use (MPEP

Section 2107.01). Thus, substantial utility is not precluded by further experimentations, and **(v)** Applicants further argues that the specification teaches that the protein encoded by SEQ ID NO: 9 may be used as an immunogen to generate antibodies which immuno-specifically bind FBP5 (page 38, lines 10 to 32). These antibodies can be used to detect aberrant FBP5 localization or aberrant levels of FBP5 in a patient tissue or serum sample (page 56, lines 21 to 27). As such, Applicants submit that the claimed invention exceeds the threshold requirement of having substantial utility.

Response to Applicant's arguments

Definitions:
[from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS; repeated from http://www.uspto.gov/web/menu/utility.pdf]

"Specific Utility" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. 101. This analysis should, of course, be tempered by consideration of the context and nature of the invention. For example, if a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.

See also the MPEP § 2107 - 2107.02.

As stated in more details in the Non-Final office action mailed on 12/01/2006, the foundation of this utility rejection was based on whether SEQ ID No: 9 and sequences that hybridize to SEQ ID No: 9 do encode a functional ubiquitin ligase, FBP5, as asserted, since the only evidence provided in the specification is that SEQ ID No: 10, asserted to be encoded by SEQ ID NO: 9, shares homology (F-box motif) to known ubiquitin ligases. -Nevertheless, Applicant's arguments regarding the uses of nucleotide sequences of SEQ ID No: 9 as probes in hybridization to FBP5, and amino acid sequences of SEQ ID No: 10 is generation of antibody that binds the asserted novel human ubiquitin ligase, FBP5, is not sufficient to overcome the rejection 35 U.S.C. 101 because the specification does not establish the asserted FBP5 (encoded by SEQ ID No: 9 with amino acid sequences of SEQ ID No; 10) is indeed a functional ubiquitin ligase of some type and being encoded by SEQ ID No: 9.

It is worth the emphasis regarding the basis for this rejection being that the specification has failed to teach any functional characterization of the claimed nucleic acid or protein encoded thereby to support that it does have ubiquitin ligase function or, importantly, what type of ubiquitin ligase it encodes such that one of skill in the art could use the claimed nucleic acid (see page 5, paragraph 2 of the office action dated 12/01/2006). Furthermore, the specification first discloses "FBP5 (SEQ ID NO: **19**)" (See line 3, page 8, and Figure 1, of specification), and then the specification further discloses "Fig. 8 A-B. **A.** Amino acid sequence of human F-box protein FBP5 (SEQ ID NO; 10). **B.** Corresponding cDNA (SEQ ID NO: 9)" (See lines 5-6, page 9 of specification). Based on the Applicant's arguments to this utility rejection in the response by Applicant filed on 06/01/2007, it appears that Applicant asserts that SEQ ID NO: 9 (not SEQ ID NO: **19**) being the cDNA that encodes amino acid sequence of human F-box protein FBP5 (SEQ ID NO: 10). In this regard, Applicant is advised to clarify whether there is any connection between SEQ ID No: 9 (and/or SEQ ID No: 19) and asserted FBP5 and be consistent throughout the specification that support the recited claims.

Claim Rejection - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

2. Claim 52 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant's arguments filed 06/01/2007 have been fully considered and they are

not persuasive. Previous rejection is ***maintained*** for the reasons of record advanced on page 12 of the office action mailed on 12/01/2006.

The term "highly stringent conditions" in claim 52 is a relative term, which renders the claim indefinite. The term " highly stringent conditions " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention.

Applicant's arguments

With regard to whether the term "highly stringent conditions" is a relative term, which renders the claim indefinite, as the term is not defined in the specification, Applicant argues that according to the applicable case law, the definiteness requirement of 35 U.S.C. § 112, second paragraph, means that the claims must have a clear and definite meaning when construed in the light of the complete patent document. Standard Oil Co. v. American Cyanamide Co., 774 F.2d 448, 227 U.S.P.Q. 293 (C.A.F.C. 1985). The test of definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification. Orthokinetic Inc. v. Safety Travel Chairs, Inc., 806 F.2d 1565, 1 U.S.P.Q.2d 1081 (C.A.F.C. 1986).

Applicant further argues that the specification as originally filed teaches that the nucleic acid molecules of the present invention can be hybridized to the complement of the DNA sequences that encode the amino acid sequences of FBP genes under highly stringent conditions (see, e.g., the specification at page 19, line 31 to page 20, line 2). By way of example, the specification teaches highly stringent hybridization conditions comprising hybridization to filter-bound DNA in 0.5M NaHP04, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C and

washing in 0.1 X SSC/0.1% SDS at 68°C. Furthermore, such methods of hybridization under highly stringent conditions were well known in the art at the time the instant application was filed (see, e.g., the specification at page 19, line 31 to page 20, line 2, citing to Ausubel et al., eds., 1989, Current Protocols in Molecular Biology, Vol. 1, Green Publishing Associates, Inc., and John Wiley & Son, Inc., New York, at p. 2.10.3).

Response to Applicant's arguments

The Examiner agrees that the term "highly stringent conditions" is commonly used in literature involving hybridization. However, there are multiple interrelated factors (including temperature, salt concentration, presence of detergent (e.g. SDS), presence of hydrogen bond competitor (e.g. formamide), time for incubation and washes etc.) that collectively determine the stringency of a given hybridization condition. The Example provides in the instant application regarded as "highly stringently conditions" could be drastically different from those conditions used by others. Accordingly, in the absence of clear definition what Applicant means by "highly stringently conditions" in the specification, the claim reciting "highly stringently conditions" reads on all other possibilities, in additional to the provided example. Thus, the metes and bounds of the phrase "highly stringent conditions" is unclear.

To demonstrate this distinction, the phrase "highly stringent conditions" for **Kuzuya et al.** is considered as following: Hybridization was performed at 52^0C for 16 h in hybridization buffer consisting of 50% formamide, 5X SSC (1X SSC contains 0.15 M NaCl and 0.015 M sodium citrate [pH 7.0]), 7% SDS, 2% blocking reagent (Boehringer), 50 mM sodium-phosphate (pH 7.0), 0.1% *N*-lauroylsarcosine, 50 μg of denatured salmon sperm DNA per ml, and 10 ng of

the digoxigenin-labeled probe per ml. After hybridization, the membranes were washed twice in 0.13 SSC containing 0.1% SDS at 688C for 15 min (See abstract, and Materials and Methods, page 3186, Kuzuya et al. Molecular analysis of outer capsid glycoprotein (VP7) genes from two isolates of human group C rotavirus with different genome electropherotypes. *J Clin Microbiol.* 34(12): 3185-9, 1996).

In conclusion, the phrase "highly stringent conditions" is a relative term, which renders the claim indefinite. Different definitions perceived by different skilled person in the art regarding what is perceived as "highly stringent conditions" for hybridization would inevitably affect what nucleotide sequences would hybridize to the sequences under investigation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 52-55 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because the claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant's arguments filed 06/01/2007 have been fully considered and they are not persuasive. Previous rejection is ***maintained*** for the reasons of record advanced on page 8-11 of the office action mailed on 12/01/2006.

Applicant's arguments

With regard to whether the claims of instant application contain subject matter that was described in the specification in such a way to convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention, Applicant argues the following: **(i)** The factual inquiry of whether there is sufficient written description under 35 U.S.C. § 112 is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, Applicant was in possession of the invention as now claimed. Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 U.S.P.Q. 2d 1111, 1117 (Fed. Cir. 1991); **(ii)** The instant specification provides clear written description for the species encompassed by FBP5. For example, the instant specification, inter alia, at page 18, lines 27-28; page 19, lines 12-14, teaches that the FBP5 gene comprises a nucleic acid molecule containing the DNA sequences as shown in Figure 8B (SEQ ID NO: 9) and any DNA sequence that encodes a polypeptide containing the amino acid sequence of FBP5 as shown in Figure 8A (SEQ ID NO: 10). The instant specification at page 19, line 31 to page 20, line 2 further teaches that the nucleic acid molecule of the present invention hybridizes to the complement of the DNA sequences that encode the amino acid sequences of an FBP protein, such as FBP5, under highly stringent conditions. Such methods of hybridization are well known in the art (see, e.g., Ausubel et al., eds., 1989, Current Protocols in Molecular Biology, Vol. 1, Green Publishing Associates, Inc., and John Wiley & Son, Inc., New York, at p. 2.10.3); **(iii)** Claim 52 is drawn to a genus of nucleic acid molecules that encodes a gene product that contains an F-box motif and binds Skp 1. It would be clear to one skilled in the art that not all sequences that hybridize to the complement of SEQ ID NO: 9 are encompassed by the claims - only those that contain an F-box motif and

bind to Skp 1. One skilled in the art would understand that the species of nucleic acid molecules that are encompassed by the claims are structurally and functionally described; **(iv)** The law does not require disclosure of a test with every species encompassed by a claim even in an unpredictable art, the specification provided an adequate description of the claimed genus. In re Angstadt, 537 F.2d 498, 502- 503, 190 USPQ 214, 216 (CCPA 1971). In fact, one skilled in the art can recite the nucleotide sequence of the nucleic acid molecules of the present invention and test the physical, chemical, and functional characteristics of the nucleic acid molecules that the claims encompass. Hence, the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date, Applicants were in possession of the invention as now claimed, **(v)** In addition to the support provided in the present specification for DNA hybridization techniques, there was a high level of skill in the art of molecular biology at the time the application was filed. All the methods needed to practice the claimed invention including DNA hybridization techniques were well known and routine in the art, and **(vi)** example 9, at page 35 of the Synopsis of Application of Written Description Guidelines, available at http://www.uspto.gov/web/patents/guides.htm ("Application Guidelines"). In Example 9 of the Application Guidelines, the specification discloses a single cDNA that encodes a protein of a particular function. A stringent hybridization was performed and several nucleic acids that encode proteins that perform the same function were isolated.

Response to Applicant's arguments

As documented in the Non-Final office action, the specification has not disclosed the sequences of any DNA sequences of mammals that are essential for hybridization under highly

stringent conditions to the nucleotide sequence of SEQ ID NO: 9; and encoding a gene product which contains an F-box motif and binds to Skp1. Regarding the breadth and variations of "highly stringent conditions", the issue has been discussed in the rejection of claim 52 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. With regard to the distinction between Example 9 of Synopsis of Application of Written Description Guidelines and claim 52 of instant application, the Examiner notes that the Example 9 provided in the Written Description Guidelines clearly defines highly stringent hybridization conditions (6X SSC and 65 degrees Celsius) in the specification whereas the definition of "highly stringent conditions" recited in claim 52 of instant application is not provided in the specification. One cannot describe what one has not conceived (in instant case, the variations in the definitions of "highly stringent conditions"). See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

It has also been noted that there is no evidence on the record of a relationship between the structures of the DNA molecules of any of the embraced mammalian DNA sequences that would provide any reliable information about the structure of DNA molecules within the genus. There is no evidence on the record that embraced sequences of any DNA sequences of from mammals that are essential for hybridization under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 9; and encoding a gene product which contains an F-box motif and binds to Skp1, had known structural relationships to each other; the art indicated that there is variation between DNA sequences of various mammalian DNA sequences that may hybridize under

highly stringent conditions to the nucleotide sequence of SEQ ID NO: 9; and encoding a gene product which contains an F-box motif and binds to Skp1 . Relevant to this issue, it is noted that the specification discloses the term "F-box motif" refers to a stretch of approximately 40 amino acid that was identified as being necessary for the interaction of F-box containing proteins with Skp1. The consensus sequence of an F-box motif is described in Bai et al., 1996, Cell 86:263-274 (See paragraph [0024], US 2005/0251871). However, the specification is silent about any assay to be performed by a skilled person in the art to analyze whether a nucleotide sequence "encodes a gene product which contains an F-box motif and binds to Skp1" as recited in step b) of claim 52. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which is not conventional in the art as of applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998).

Accordingly, in the instant case the claimed embodiments of an isolated nucleic acid sequence derived from a mammalian genome hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 9; and encodes a gene product which contains an F-box motif and binds to Skp 1 lack a written description. The specification fails to describe what DNA molecules fall into this genus because there is no definition of "highly stringent conditions and there is no assay described to analyze whether a nucleotide sequence "encodes a gene product which contains an F-box motif and binds to Skp1". The skilled artisan cannot envision

the detailed chemical structure of the encompassed regulatory elements, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

In view of the above considerations one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by member of the genus of nematode regulatory elements. Moreover, the art has recognized that there would be variation among the species of the genus of DNA sequences of mammal as such DNA sequences appear to be specific for particular genes from different species of mammal. Therefore, Applicant was not in possession of the genus of all DNA sequences of from all mammals that hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 9; and encodes a gene product which contains an F-box motif and binds to Skp1 as encompassed by the claims. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention."

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Previous rejection of claims 51-55 under 35 U.S.C. 102(b) as being anticipated by NCI-CGAP http://www.ncbi.nlm.nih.gov/ncicgap (See National Cancer Institute, Cancer Genome Anatomy Project (CGAP), Tumor Gene Index, 1997), is ***withdrawn*** because Applicant's arguments filed 06/01/2007 have been fully considered and they are persuasive.

The rejection was based on that NCI-CGAP http://www.ncbi.nlm.nih.gov/ncicgap teaches a *cDNA clone* of Rhesus monkey (*Macaca multta*) that matches the SEQ ID 9, with SEQ ID 9 nucleotide Nos from 605 to 1329 being 98.3% identical to the nucleotide sequences from 3 to 727 of NCI-CGAP http://www.ncbi.nlm.nih.gov/ncicgap database.

Applicant argues that the nucleic acid sequence of GenBank Accession No. CB229742 did not become available to the public until February 10, 2003, which is after the priority date of the present application. Hence, NCI-CGAP is not prior art to the claimed subject matter, and the Examiner agrees.

5. Previous rejection of claims 51-55 under 35 U.S.C. 102(b) as being anticipated by Bonaldo et al. (See sequence search result listed below, Bonaldo et al. Normalization and subtraction: two approaches to facilitate gene discovery. *Genome Res.* 6 (9), 791-806, 1996), is

withdrawn because Applicant's arguments filed 06/01/2007 have been fully considered and they are persuasive.

The rejection was based that Bonaldo et al. also teach the construction and preliminary characterization of a subtracted liver/spleen library (INFLS-SI) that resulted from the elimination (or reduction of representation) of 5000 INFLS-IMAGE clones from the INFLS library (See abstract), and nucleic acid sequence search of SEQ ID No. 9 aligned with the human nucleic acid sequences taught by Bonaldo et al.

Applicant argues that the cited GenBank accession No. BM675277, the nucleic acid sequence of which did not become available to the public from GenBank until February 27, 2002. Hence, GenBank accession No. BM675277 is not prior art to the claimed subject matter, and the Examiner agrees.

6. Previous rejection of claims 51-55 under 35 U.S.C. 102(e) as being anticipated by Williams et al. (U.S. application No. 09/297,648, U.S. Patent No. 6,964,868, date of Patent, Nov. 15, 2005, which is an U.S. application No. 09/297,648. The application is the National Phase under 35 U.S.C. 371 of International Application No. PCT/US99/01619, filed Jan. 28, 1999), is ***withdrawn*** because Applicant's arguments have been fully considered and found persuasive.

Specifically, with regard to Williams et al. being qualified as an 102(e) prior art, Applicant argues that the support for the present claims is found in the parent application, U.S. Application Serial No. 09/385,219, filed August 27, 1999, now U.S. Patent No. 6,720,181. Williams was a National Stage Application of PCT/US99/01619, which was filed January 28, 1999. The critical reference date of Williams is when the applicant has fulfilled the requirements

of paragraphs (1), (2), and (4) of 35 U.S.C. § 371(c), i.e., March 10, 2000. According to MPEP 2136.03(III), international applications which were filed prior to November 29, 2000 may not be used to reach back (bridge) to an earlier filing date through a priority or benefit claim the prior art purposes under 35 U.S.C. § 102(e). Hence, Williams is not prior art to the claimed subject matter, and the Examiner agrees.

7. Claims 51-55 are rejected under 35 U.S.C. 102(b) as being anticipated by **Skowyra et al.** (Skowyra et al., F-box proteins are receptors that recruit phosphorylated substrates to the SCF ubiquitin-ligase complex. *Cell*, 91(2): 209-19, 1997).

With regard to the limitation of an isolated nucleic acid molecule which encodes an F-box polypeptide, or a fragment thereof recited in claim 51, Skowyra et al. teach the reconstitution of the ubiquitination pathway for the Cdk inhibitor Sic1 using recombinant proteins (which inherently reads on isolated nucleic acid encoding the recombinant proteins). Skp1, Cdc53, and the F-box protein Cdc4 form a complex, SCFCdc4, which functions as a Sic1 ubiquitin-ligase (E3) in combination with the ubiquitin conjugating enzyme (E2) Cdc34 and E1. Cdc4 assembled with Skp1 (which reads on the limitation "binds to Skp1" recited in claim 52) functions as the receptor that selectively binds phosphorylated Sic1. Grr1, an F-box protein involved in Cln destruction, forms complexes with Skp1 and Cdc53 and binds phosphorylated Cln1 and Cln2, but not Sic1 (See abstract, Skowyra et al., 1997).

With regard to the limitation said nucleic acid molecule comprising *a* nucleic acid sequence of SEQ ID No: 9 recited in claim 51, it is noted that the limitation reads on any fragment of nucleotide sequence of SEQ ID No: 9, including ATG, which is the initiation codon

required for initiation of translation of recombinant F-box motif containing recombinant proteins taught by Skowyra et al. Furthermore, the coding sequences (120 nucleotides) corresponding to the F-box motif (40 amino acids) present in the recombinant proteins (for instance, Cdc4, Grr1 etc) would hybridize under stringent conditions to the nucleotide sequence of SEQ ID No: 9, as recited in claim 52. It is noted that, bearing broadest and reasonable interpretation in mind, the phrase "a nucleotide sequence *derived from* a mammalian genome" recited in claim 52, reads on functional homologous genes corresponding to the mammalian genes in other eukaryotic organisms (including yeast, as taught by Skowyra et al., 1997).

With regard to expression vector and host cell (claims 53-55 of instant application), Skowyra et al. teach baculoviruse vectors expressing various F-box motif-containing proteins (See Table 1, page 218, Skowyra et al., 1997) in an insect cell line named Hi5 (See Experimental procedures, page 217, Skowyra et al., 1997).

Thus, Skowyra et al., 1997 clearly anticipates claims 51, and 53-55 of instant application.

Conclusion

8. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to Dianiece Jacobs whose telephone number is (571) 272-0532.

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